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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,226	01/22/2001	Osamu Ohara	2534USOP	5358

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EXAMINER
WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/13/2002 //

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/744,226	OHARA ET AL.	
	Examin r	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *3-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-16* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, sent 21 May 2001, has been entered as Paper 8. Applicant's election of Invention I (Claims 1 and 2) in Paper No. 10 (23 October 2002) is acknowledged. In addition, Applicant elected the following: The polypeptide of SEQ ID NO: 1. Applicants elected Invention I with traverse, asserting that the polynucleotides and antibodies of Inventions II and III are sufficiently related to be included in the examination of Invention I. However, Inventions I, II and III were properly restricted as separate compositions having characteristic differences in structure and function and each having an independent utility which cannot be exchanged. Furthermore, since a complete search of the art includes a search of the art that renders an invention obvious as well as anticipatory, the additional searches required for examination of Inventions I *with* Inventions II and III would be extensive, thus presenting an undue burden for the examiner.

Claims 3-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim.

Claims 1 and 2 are under examination in the current application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "HUMAN G-PROTEIN COUPLED SECRETIN-LIKE RECEPTOR".

Appropriate correction is required.

Sequence Rules

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules is not accompanied by the required reference to the relevant sequence identifier (i.e., SEQ ID NO:). This happens in Figures 1, 2, 4, 5 and 7-24, for example.

Abstract

The Abstract is objected to for consisting of two paragraphs. It should consist of one paragraph of 25 lines or less and 150 words or less.

Appropriate correction is required.

Claim Rejections/Objections

Claim Objections

Claim 1 is objected to for reciting non-elected subject matter (SEQ ID NO: 3 and 5).

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of 35 U.S.C. 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to the peptide of SEQ ID NO: 1, as well as fragments and salts of SEQ ID NO: 1.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed polypeptides:

1) To search for drugs as ligands or antagonists of the polypeptide of SEQ ID NO: 1,

2) To make hybridization probes and primers to detect nucleic acid molecules that encode the polypeptide of SEQ ID NO: 1 and to localize gene expression in tissue samples,

3) In the creation of transgenic animals,

4) For gene therapy,

5) As drugs for the treatment or prevention of ligand polypeptide deficiency,

6) To detect relevant polymorphisms in individuals, and

7) For the production of antibodies.

Each of these shall be addressed in turn:

1) To search for drugs as ligands or antagonists of the polypeptide *of SEQ ID NO: 1.* This asserted utility is credible and specific. However, it is not substantial. The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure for example, of how to assay for possible transduction mechanisms. If relying on the Specification, it is not known the class of drugs to use or what measurements to perform. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not substantial.

2) To make hybridization probes and primers to detect nucleic acid molecules that encode the polypeptide of SEQ ID NO: 1 and to localize gene expression in tissue samples. This

asserted utility is credible but not substantial or specific. Hybridization probes and primers can be designed from any polynucleotide sequence. Further, the instant Specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) In the creation of transgenic animals. This asserted utility is credible but not specific or substantial. The specification does not disclose diseases associated with a mutated, deleted, or translocated gene of the present invention. Significant further experimentation would be required of the skilled artisan to identify such a disease. The instant Specification discloses nothing about whether the claimed gene will be "knocked in" or "knocked out" or what specific tissues and cells are being targeted. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) For gene therapy. This asserted utility is credible but not specific or substantial. Such can be performed for any polynucleotide encoding a receptor. Further, the instant Specification does not disclose diseases associated with a mutated, deleted, or translocated gene of the claimed invention. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease and to determine the route of administration of the gene, as well as quantity and duration of treatment. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5) As drugs for the treatment or prevention of ligand polypeptide deficiency. This asserted utility is credible and specific, however, it is not substantial. The instant Disclosure does not disclose any conditions wherein there is a deficiency of the claimed polypeptide.

Significant further experimentation would be required of the skilled artisan to identify individuals who would benefit from such a drug, and then to determine a best course of treatment. There is no disclosure, for example, of dosages, how to assay for improvement or intolerable levels of side effects, etc. Since this asserted utility is not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

6) To detect relevant polymorphisms in individuals. This asserted utility may be credible, however it is neither specific nor substantial. Generally, the well-known polymorphisms referred to by the applicant occur in metabolic enzymes (e.g. the liver P450's or the dehydrogenases), and are very well characterized physiologically and within populations. Applicants have not demonstrated the function of the polypeptide encoded by the claimed polynucleotide, much less clinically relevant polymorphisms. Thus, the asserted utility is not substantial. Finally, many unrelated sequences can be polymorphic, generally. Thus, the asserted utility is not specific.

7) *For the production of antibodies.* This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the instant Specification discloses nothing specific and substantial about the polypeptide, both the polypeptide and its antibodies have no patentable utility.

Claims 1 and 2 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the Invention.

The claims are directed to the peptide of SEQ ID NO: 1, as well as fragments and salts of SEQ ID NO: 1.

The specification teaches the polypeptide of SEQ ID NO: 1. However, the specification does not teach functional or structural characteristics of the polypeptide recited in the claims.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the prôtein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Numerous examples from the receptor art demonstrate polypeptides with high homology having a wide-variety of functions in organisms (Ji, et al, 1998, JBC, 273:17299). Even closely-related family members sometimes work very differently and have different specific functions in the organism (Ji, et al, 1998, p. 17302, 3rd paragraph; Probst, et al,

1992, DNA and Cell Biol, 11: 1-20). This indicates that one skilled in the art would not know the utility and function of the claimed polypeptide, even if it were definitively classified as a neuromedin or secretin-like G-protein coupled receptor. Finally, Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the Applicant's Specification fails to teach the skilled artisan how to use the disclosed polynucleotide to make a biologically active polypeptide without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polypeptide for *any* purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polypeptide could be used as a diagnostic tool. There are no data in the Specification concerning ligands for the receptor, or transduction processes, or any other processes or functions specific to this receptor. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polypeptide for any purpose.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence

or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polypeptide of SEQ ID NO: 1 and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarities, the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Furthermore, Regarding Claim 2, the specification does not enable fragments or "partial peptides" of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims.

The claim is directed to fragments and variants of SEQ ID NO: 1. Claim 2 reads on "partial peptides" of SEQ ID NO: 1. The scope of the patent protection sought by the Applicant as defined by the claim fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

The Instant Application does not reasonably provide enablement for various protein forms of SEQ ID NO: 1, wherein the claimed protein includes "partial peptides" of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The specification is not enabled for the full scope of the protein, wherein the amino acid sequence is a "partial peptide" of SEQ ID NO: 1, with the assurance that enabled proteins can be made without undue experimentation and with the assurance that they would have the desired properties. There are no examples of what specific polypeptides fall within the range of those that would be a "partial peptide" of SEQ ID NO: 1. In fact, a short sequence of 2 or 3 amino acids from SEQ ID NO: 1 would constitute a "partial peptide". Neither is it clear if the fragment need be contiguous, or over a specific portion of the protein of SEQ ID NO: 1.

Due to the large quantity of experimentation required to determine how to use fragments of SEQ ID NO: 1, the lack of direction or guidance in the specification regarding the specific activity of the polypeptide of SEQ ID NO: 1, the lack of working examples to fragments of SEQ ID NO: 1, the state of the art showing the unpredictability of function based on structure, and the breadth of the claim which embrace innumerable variants of the polypeptides of SEQ ID NO: 1 - undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. 102(b) as being unpatentable over Baud, et al, 1995, Genomics, 26(2): 334-344. Baud et al. disclose a polypeptide sequence which is approximately 70% identical to SEQ ID NO: 1 in the instant application. This reference meets the limitations of claim 2 of "a partial peptide" of the protein of Claim 1, which includes, for example, small and large fragments of SEQ ID NO: 1.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, -second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "substantially" in claim 1 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not

provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Conclusion: Claims 1 and 2 are rejected for the reasons listed above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

SLW

ELIZABETH KEMMERER
PRIMARY EXAMINER

12/9/02